REMARKS

Claims 1 to 4 and 7 are pending in the present patent application. Claims 1 to 4 have been amended. Claims 5 and 6 have been withdrawn in view of the election/restriction requirement dated February 10, 2005, without prejudice to their presentation in a later-filed divisional patent application.

In view of the foregoing amendments and the following remarks, reconsideration and withdrawal of the rejections are respectfully requested.

Clarification of Applicants' Position With Respect to the Restriction Requirement

Although the restriction requirement has been made final, Applicants wish to clarify their position with respect to their traversal of the restriction requirement as set forth in the Reply filed March 8, 2005. In their Reply, Applicants did ***not*** argue that the restriction requirement was improper because the claims were ***allowable***, as is alleged at page 2 of the Action. Rather, in response to the Examiner's allegations that searching all of the claims together would be unduly burdensome, Applicants pointed out that the claims ***had already been searched together*** and, as evidence of such search, they were all indicated to be allowable. In this regard, page 3 of the Office Action dated September 22, 2004, clearly indicates that claim 6, one of the claims separated from claims 1 to 4 and 7 by the present Examiner, was ***allowable*** (notwithstanding the present Examiner's position with respect to the allowability of such claims). Thus, the fact that claim 6 was previously indicated as allowable along with claims 1, 3, and 4, strongly undermines the Examiner's position that it would be unduly burdensome to search claim 6 with, for example, claims 1, 3, and 4, because such search has apparently already been performed by the office; otherwise, claims 1, 3, 4, and 6 would not have been indicated as being allowable.

Discussion of the Rejection Under 35 U.S.C. § 102

Claims 1 to 4 and 7 have been rejected under 35 U.S.C. § 102(a), (b), and (e) as allegedly being anticipated by Example 137 of WO 02/088073 and U.S. published patent application No. 2003/0187033, both to Brendel ("the Brendel references") in view of the teaching in the Brendel references that Brendel relates to the use of all possible enantiomers of the compounds disclosed therein. Applicants respectfully traverse this rejection because the Brendel references do not disclose each and every claim element.

Applicants' claims define a composition ***consisting of*** 2-(Butyl-1-sulfonylamino)-N-[1(R)-(6-methoxypyridin-3-yl)propyl]benzamide of the formula I or its physiologically tolerable salts. The corresponding (S) enantiomer, 2-(Butyl-1-sulfonylamino)-N-[1(S)-(6-methoxypyridin-3-yl)propyl]benzamide, is not included within the scope of the pending claims by virtue of the "consisting of" recitation.

In contrast, Example 137 of the Brendel references discloses a racemic ***mixture*** of both enantiomers of the compound. In this regard, the Brendel references disclose that Example 137 was prepared according to General Method 6. General Method 6, in turn, is not a stereo specific method such as that defined by claim 7 wherein the stereo specific amine, (R)-(6-methoxypyridin-3-yl)propylamine, is employed in the synthesis. Since General Method 6 is not stereo specific, and it does not specify that a particular enantiomer is separated from the mixture, there is no evidence of record to support the assertion in the Action that Example 137 of the Brendel references anticipates any of the pending claims. Thus, since Example 137 of the Brendel references does not disclose a composition ***consisting of*** 2-(Butyl-1-sulfonylamino)-N-[1(R)-(6-methoxypyridin-3-yl)propyl]benzamide, but rather a composition that is a mixture of 2-(Butyl-1-sulfonylamino)-N-[1(R)-(6-methoxypyridin-3-yl)propyl]benzamide ***and*** 2-(Butyl-1-sulfonylamino)-N-[1(S)-(6-methoxypyridin-3-yl)propyl]benzamide, the Brendel references do not anticipate Applicants'

claimed invention. Accordingly, reconsideration and withdrawal of the rejection in view of the Brendel references are requested respectfully.

Discussion of the Rejection Under 35 U.S.C. § 103(a)

Claims 1 to 4 and 7 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over the Brendel references. Applicants respectfully traverse this rejection as there is nothing in the Brendel references that would teach or suggest to one of ordinary skill in the art that the (R) enantiomer, 2-(Butyl-1-sulfonylamino)-N-[1(R)-(6-methoxypyridin-3-yl)propyl]benzamide, alone is surprisingly superior in the inhibition of the occurrence of episodes of arrhythmias relative to the racemic mixture or to the (S) enantiomer alone despite IC_{50} values that suggest the contrary.

In this regard, the IC_{50} values were determined for the following subject compounds:

	Compound	IC_{50} Values
1.	2-(Butyl-1-sulfonylamino)-N-[1-(6-methoxypyridin-3-yl)propyl]benzamide (Racemic mixture)	2.4 μM
2.	2-(Butyl-1-sulfonylamino)-N-[1(R)-(6-methoxypyridin-3-yl)propyl]benzamide	10 μM
3.	2-(Butyl-1-sulfonylamino)-N-[1(S)-(6-methoxypyridin-3-yl)propyl]benzamide	2.4 μM

(*see*, Applicants' specification at pages 13 to 14). This data suggests that that the racemic mixture or the pure (S)-enantiomer (3) would be superior to the pure (R) enantiomer (2) because significantly less of the racemic mixture or the pure (S) enantiomer was needed to achieve a 50% inhibitory concentration of the Kv1.5 control current relative to the (R) enantiomer. As it turns out, however, Applicants have surprisingly discovered that, of the two enantiomers, the (R) enantiomer far out performed the (S) enantiomer in an investigation

into the ability of the compounds to prolong the refractory period and anti-arrhythmic activity on the left atrium of an anesthetized pig.

Applicants detail, at pages 14 to 15 of the present specification, that a comparison of the action of 2-(butyl-1-sulfonylamino)-N-[1(R)-(6-methoxypyridin-3-yl)propyl]benzamide of the formula I and 2-(butyl-1-sulfonylamino)-N-[1(S)-(6-methoxypyridin-3-yl)propyl]benzamide on the refractory period of the left atrium and antiarrhythmic activity in the anesthetized pig after a bolus administration of 3 mg/kg clearly demonstrates that the (R) enantiomer causes a markedly greater prolongation of the refractory period than the (S) enantiomer. Significantly, Applicants found that, by using the (R) enantiomer, it was possible to prevent *73.9%* of the induced arrhythmias, while when using the (S) enantiomer, the occurrence of arrhythmias was inhibited only by *27%*. Moreover, as shown in Figure 1 of Applicants' specification, 2-(butyl-1-sulfonylamino)-N-[1(R)-(6-methoxypyridin-3-yl)propyl]benzamide led to a longer-lasting action on the left-atrial refractory period, which also continued unchanged for 180 minutes after ending the infusion. Indeed, there is no teaching or disclosure in the Brendel references that would allow one skilled in the art to predict or to expect these advantages. Accordingly, reconsideration and withdrawal of the rejection for alleged obviousness in view of the Brendel references is requested respectfully.

Discussion of the Rejection Under 35 U.S.C. § 112, First Paragraph

Claim 3 has been rejected under 35 U.S.C. § 112, first paragraph as allegedly lacking enablement for the prevention of arrhythmias and flutters. Applicants traverse this rejection because one skilled in the art having read the present specification and claims would be able to make and use the present invention with respect to the prevention of arrhythmias and flutters without engaging in undue experimentation.

It is settled law that whenever the adequacy of enablement provided by an applicant's specification is challenged, the examiner has the initial burden of giving reasons, supported by the record as a whole, why the specification is not enabling. *In re Armbruster*, 185 U.S.P.Q. 152 (C.C.P.A. 1975). The enablement requirement of 35 U.S.C. §112 is satisfied if a disclosure contains sufficient information such that persons of skill in the art, having the disclosure before them, would be able to make and use the invention. The legal standard for enablement under §112 is whether one skilled in the art would be able to practice the invention without undue experimentation. *In re Wands*, 8 U.S.P.Q. 1400 (Fed. Cir. 1988).

The Examiner has acknowledged the actual, working examples in the instant patent application to the extent that they relate to the treatment of cardiac arrhythmias, supraventricular arrhythmias, atrial fibrillation or atrial flutters. The Examiner, however, alleges that such examples do not provide guidance to one of ordinary skill in the art with respect to the prevention of these conditions. Indeed, a closer look at Applicants' working examples demonstrates that the examples are illustrative of the ***full breadth*** of the inventions and are supportive of enablement of the ***full scope*** of the claims, not the limited scope attributed by the Examiner.

In this regard, one of ordinary skill in the art to which the present invention is directed knows that inhibition of Kv1.5 represents an effective method for prolonging the artrial action potential and, thus, for ending or preventing atrial arrhythmias. Moreover, the working examples in Applicants' specification demonstrate such prevention. As detailed above, pages 14 to 15 of Applicants' specification demonstrate that, by using the (R) enantiomer, it was possible to ***prevent 73.9%*** of the induced arrhythmias, while when using the (S) enantiomer, the occurrence of arrhythmias was inhibited only by *27%*. Moreover, as shown in Figure 1 of Applicants' specification, 2-(butyl-1-sulfonylamino)-N-[1(R)-(6-methoxypyridin-3-yl)propyl]benzamide led to a longer-lasting action on the left-atrial

refractory period, which also ***continued unchanged*** for 180 minutes after ending the infusion. Thus, Applicants' specification provides an enabling disclosure that is commensurate to the full scope of claim 3. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

Discussion of the Rejection Under 35 U.S.C. § 112, Second Paragraph / 35 U.S.C. § 101

Claim 4 has been rejected under 35 U.S.C. § 112, second paragraph and under 35 U.S.C. § 101 as allegedly being indefinite for defining a method of use that does not involve any steps. Applicants respectfully traverse this rejection.

Claim 4 is not a method of use claim. Claim 4 is a composition claim that defines a "pharmaceutical preparation [*i.e.*, composition] for human or veterinary use." Since claim 4 is not a "method" claim, process steps are not required. Claim 4, therefore, is not indefinite. Accordingly, reconsideration and withdrawal of the rejection are requested respectfully.

Discussion of the Provisional Double Patenting Rejection

Claims 1 to 4 and 7 have been provisionally rejected under the judicially-created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 7, 8, 10 to 14, and 19 to 24 of commonly-owned co-pending Application No. 10/132,163. Applicants request that this rejection be deferred pending some identification of allowable subject matter, as it likely can be readily resolved (depending upon the subject matter ultimately allowed) through the filing of a suitable terminal disclaimer.

Conclusion

The foregoing is submitted as a full and complete response to the Action mailed on April 25, 2005, and the allowance of all claims is respectfully requested. If there are any issues that can be resolved by a telephone conference or an Examiner's amendment, the Examiner is invited to call the undersigned attorney at (908) 231-3410.

The Commissioner is hereby authorized to charge the fee required and any additional fees that may be needed to Deposit Account No. **18-1982** in the name of Aventis Pharmaceuticals Inc.

Respectfully submitted,

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